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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/067,991 | 02/08/2002 | Vincent Fischetti | NH-Comp Strep | 9941 |

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| EXAMINER | |
|---|---|
| PRATS, FRANCISCO CHANDLER | |
| **ART UNIT** | **PAPER NUMBER** |
| 1651 | |

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/067,991 | FISCHETTI ET AL. | |
| | Examiner | Art Unit | |
| | Francisco C Prats | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *8,10-19 and 46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8, 10-19 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**DETAILED ACTION**

The amendment filed March 15, 2004, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 8, 10-19 and 46 are pending and are examined on the merits.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 10-19 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the language "lysin enzyme characterized by the ability to destroy only the cell wall of a bacteria selected from the group consisting of [of] Group A Streptococci, Group C Streptococci, and Group E

Streptococci" raises two new matter issues. First, the specification as originally filed does not mention a lysin enzyme specific for Group E streptococci. Thus, the specification as originally filed does not provide support for the new language reciting such an enzyme.

Second, the specification as filed states that the lysin enzyme produced by group C streptococci is specific for lysing group A streptococci. See specification at page 9, lines 3 and 4. ("When group C Streptococci are infected with a C1 bacteriophage, a lysin enzyme is produced specific for the lysing of Streptococcus group A.") Properly assuming that the group C phage lysin lyses group C streptococci in addition to group A streptococci, this disclosure in the specification does not support the new recitation in the claims that the enzyme destroys "only" the cell wall of group A ***or*** group C streptococci. That is, the claim as amended recites an enzyme which destroys only group A or group C streptococci cell walls, whereas the specification as originally filed clearly discloses that the group C phage lysin destroys both group A and group C streptococcal cell walls. A holding of new matter is therefore required. Note that deletion of the word "only" would resolve the second of the two new matter issues raised by applicant's amendment.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8, 10-12, 18, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa et al (U.S Pat. 3,786,141) in light of Sokawa et al (J. Biochem. 57(1):64-74 (1965)).

As amended, the claims recite compositions comprising two ingredients (1) a phage-encoded lysin enzyme capable of destroying the cell walls of Group A streptococci, and (2) a nasal spray carrier.

Ogawa discloses the preparation of "a lytic enzyme prepared from the lysate of Bacteriophage ATCC No. 21597-b-infected Group C Streptococcus sp. ATCC NO 21597, according to the method

described in the Journal of Biochemistry, vol. 57, p. 67 (1965)." See column 4, lines 7-11. Thus, Ogawa discloses the preparation of an enzyme from the identical phage strain used by applicant, using the identical host bacterial strain as applicant. See applicant's specification at page 26, lines 1-10; compare applicant's strains to Ogawa's.

Ogawa uses the disclosed enzyme preparation to lyse microorganisms (see Example 1 of Ogawa), so it is not clear from Ogawa whether the lysin preparation, prior to its use, is in an aqueous carrier solution suitable for administration according to applicant's claims. However, Sokawa, the article clearly referred to by Ogawa, clearly discloses on page 65 that the precipitated enzyme preparation is "dissolved in M/75 phosphate buffer, pH 7.0, and lyophilized after dialysis against the same buffer in the cold." Sokawa, page 65, left column, second full paragraph. Thus, because Ogawa discloses that the enzyme preparation was made according to the disclosure of Sokawa, it is clear that Ogawa's enzyme preparation, prior to its use, was in an aqueous buffer solution, as required by applicant's claims. Moreover, in view of the fact that Ogawa used the same strains of phage and bacterium as used by applicant, there is no doubt that the prior art enzyme has the same activity as recited in the claims. Lastly, note that the presence of the enzyme in

an aqueous buffered medium reads on the presently claimed nasal spray, since aqueous compositions clearly can be administered as sprays. A holding of anticipation over the cited claims is clearly required.

Claims 8, 10-12, 14, 15 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Raina (J. Bacteriol. 145(1):661-663 (1981)).

Raina describes the purification of a lysin enzyme from Streptococcus Group C bacteriophage, a bacteriophage encompassed by the claimed strain. See abstract. The bacteriophage, in various stages of purification, is described as being present in several different aqueous buffer solutions comprising various buffers and/or agents encompassed by the claims including phosphate, EDTA and mercaptoethanol. See, e.g., sentence spanning left and right columns on page 661. Note that because any aqueous solution can be administered in spray form, any aqueous solution can be considered a nasal spray carrier. Thus, Raina describes a composition comprising the claimed ingredients. A holding of anticipation over the cited claims is required.

Claims 8, 10-18 and 46 are rejected under 35 U.S.C. 102(a) or 102(e) as being anticipated by Fischetti et al (U.S. Pat. 5,604,109).

Fischetti describes compositions comprising the claimed enzyme, produced by culturing the same phage strain on the same bacterial strain as disclosed in the instant specification at page 26. See column 4, lines 15-65 (Example 1). The enzyme preparation is disclosed as being in the same buffer systems, in lyophilized form, as recited in the claims. Note that because any aqueous solution and/or powder can be administered in spray form, any aqueous solution can be considered a nasal spray carrier. Because Fischetti describes a composition comprising the claimed ingredients, and because the described compositions can be applied to the presently claimed use (i.e., nasal spray), a holding of anticipation over the cited claims is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the

art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raina (J. Bacteriol. 145(1):661-663 (1981)) or Fischetti et al (U.S. Pat. 5,604,109) in view of Roser (U.S. Pat. 4,891,319).

As discussed above, each of Raina and Fischetti discloses compositions comprising the claimed enzyme in an aqueous carrier system which can be administered according to the claimed intended uses. Neither Raina nor Fischetti discloses combining the enzyme compositions with a sweetener, as recited in claims 19 and 36. However, Roser clearly discloses that the sweetener trehalose is highly advantageous for use as an enzyme preservative. Thus, the artisan of ordinary skill, recognizing Roser's disclosure of the advantages of using trehalose for enzyme stabilization, clearly would have been motivated to have combined the enzyme disclosed by Raina and Fischetti with

trehalose to have formed a stabilized enzyme composition. A holding of obviousness is clearly required.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8, 10-19 and 46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 5,997,862, over claims 1-28 of U.S. Patent No. 6,017,528, claims 22-49 of U.S. Patent No. 6,056,955, claims 1 and 2 of U.S. Patent 6,277,399, and claims 1-10 of U.S. Patent. 6,423,299.

With respect to the '862 patent, although the conflicting claims are not of identical scope, they are not patentably distinct from each other because the patented claims recite

subject matter which is entirely encompassed by the instant claims. Moreover, a pharmaceutical composition comprising a lysin enzyme produced by phage C1 clearly suggests the "lysin enzyme genetically coded for by a bacteriophage" generically claimed in claim 31 herein. Thus, although the claims under examination contain subject matter broader than the patented subject matter, the claims under examination encompass subject matter clearly suggested by the subject matter previously patented by applicant. A terminal disclaimer is therefore clearly required.

With respect to the '528 patent, although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed use of a mammal in the '528 patent renders obvious the generic use claimed herein, which encompasses treatment of a mammal. With respect to the '955, '399 and '299 patents, it is noted that certain of the patented claims recite the carriers in terms of intended uses which are different than the intended uses recited in the claims under examination herein. However, because liquid solutions, can be used in a variety of different administration modes, including the presently claim nasal spray application, the patented claims recite overlapping subject matter clearly suggesting the subject matter recited in the claims under examination. Because the

patented claims suggest the subject matter claimed in the instant application, a terminal disclaimer is clearly required.

***Response to Arguments***

All of applicant's argument has been fully considered but is not persuasive of error. Applicant urges that none of the prior art references teaches anything about a nasal spray, and that therefore the references neither anticipate nor render obvious the nasal spray recited in the claims as amended. However, applicant's argument ignores the fact that every prior art reference cited herein discloses the claimed enzyme in an aqueous solution. Aqueous solutions can be administered by spraying. One need only place the solution in a spray device and use it to administer the enzyme-containing solution.

Applicant urges that a nasal spray is an aerated spray containing a number of components in a special container geared to distribute the lytic enzyme into the patient's nose. However, applicant's argument ignores the fact that at their broadest the claims require only two ingredients, an enzyme and a nasal spray carrier. These two ingredients, and other claimed ingredients as discussed above, are present in all of the cited prior art. Because the prior art compositions are aqueous solutions comprising enzyme, they can be administered as a nasal

spray. The prior art compositions must therefore be considered anticipatory of the claimed compositions.

To the extent that a special container is required for administering the composition to the patient, note that no such container is recited in the claims. That is, applicant is arguing about limitations not present in the claims. Moreover, to the extent that applicant argues that the prior art compositions cannot be administered as nasal sprays, applicant is essentially arguing about an intended use for the claimed compositions. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Again, because the prior art compositions can be administered as nasal sprays, a holding of anticipation is clearly required.

Lastly, while the proffer of a terminal disclaimer is noted, the obviousness-type double patenting rejections cannot be withdrawn until the terminal disclaimer is actually filed.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Francisco C Prats
Primary Examiner
Art Unit 1651

FCP